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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,000	02/17/2005	Roland Suck	MERCK-2975	2809

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
05/13/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,000	SUCK ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-21 and 23* is/are pending in the application.

4a) Of the above claim(s) *7-11,16 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6, 12-15, 17* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/06/2008 has been entered.

2. Claims 6-21 and 23 are pending.

3. Claims 7-11, 16 and 18-21 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/17/2007.

4. Claims 6, 12-15, 17 and 23 are currently under examination as they read on a Phl p 1 variant characterized in that it has an additional cysteine residue as compared with the wild type.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 6, 12-15 and 17 *are* rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: the polypeptide of SEQ ID NO:2, the polypeptide of SEQ ID NO:2 with a His tag and the LM and HM fold variants of SEQ ID NO:2, the specification does not provide reasonable enablement for: a polypeptide variant of major allergen Phl p 1 from timothy grass which comprises an additional Cys residue compared to the wild type Phl p 1 sequence, said polypeptide variant **comprising a polypeptide sequence set forth in SEQ ID NO: 2**, wherein the additional Cys residue has been introduced by exchange of Ala 236 of claim 6; which exists in various fold forms of claim 12; a fold form rPhl p 1-LM of **the polypeptide variant according to claim 6**, which is obtainable by: (a) overexpressing in a host organism, a fusion protein comprising the rPhl p 1 polypeptide variant and a His tag; (b) denaturing inclusion bodies isolated from the host organism using guanidinium chloride; (c) renaturing dissolved protein on a chelate affinity chromatography column; (d) removing the His tag; (e) employing gel filtration; (f) further purifying using chelate affinity chromatography; (g) isolating the target protein from the flow-through; and (h) further employing gel filtration of claim 13; a fold form rPhl p 1-HM of **the polypeptide variant according to claim 6**, which is obtainable by: (a) overexpressing in a host organism, a fusion protein comprising the rPhl p 1 polypeptide variant and a His tag; (b) denaturing inclusion bodies isolated from the host organism using guanidinium chloride; (c) renaturing dissolved protein on a chelate affinity chromatography column; (d) removing the His tag; (e) employing gel filtration; (f) further purifying using chelate affinity chromatography; (g) eluting the target protein with an imidazole gradient; and (h) further employing gel filtration of claim 14; a **vaccine** which comprises **the**

polypeptide variant according to claim 6 and an acceptable carrier of claim 15; and a **pharmaceutical composition** comprising **a polypeptide variant according to claim 6** and a pharmaceutically acceptable carrier of claim 17 for the same reasons as set forth in the Office Action mailed on 07/22/2008.

Applicant's arguments filed on 11/06/2008 have been fully considered, but are not found persuasive.

Applicant argues:

> "At page 7 of the Office Action, it is alleged that "the specification only disclosed [sic] the Phl p 1 allergen mutant *consisting* of SEQ ID NO: 2." Again at page 13, the Office Action contends that "Applicant is in possession of a Phl p 1 allergen mutant *consisting of* SEQ ID NO: 2." These contentions are both incorrect. The specification, for example, in the disclosure contained in Examples 1 and 2 discloses synthesis and purification of polypeptides in native-form (i.e., untagged) and in fusion-form (i.e., His-tagged). The activity of such molecules, for example, with respect to IGE reactivity, is further described in page 17 of the specification. As such, the present specification provides a detailed description of the claimed subject matter (for example, polypeptides *comprising* SEQ ID NO: 2 and/or uses thereof). Moreover, the disclosure therein enables one of ordinary skill in the art to *make and use* the claimed invention in its broadest possible scope. Withdrawal of this contention is respectfully requested.
>
> With respect to the fold-forms of the Phl p 1 polypeptides claimed herein (see, claims 13 and 14), it is respectfully submitted that the specification provides a detailed disclosure of the characteristics thereof, including methods for making and using such molecules in a manner described in the claims. See, for example, the disclosure contained in Figures 1-3 and the description thereof at page 5 of the originally-filed specification.
>
> With regard to the other outstanding allegations of non-enablement, Applicants respectfully disagree with the PTO's contentions. However, in order to facilitate prosecution, the claims have been amended. It is submitted that the forgoing amendments render the rejections under 35 U.S.C. 112, ¶1 moot. Withdrawal of the rejection is respectfully requested."

It is the Examiner's position that the specification has not adequately disclosed a polypeptide variant "comprising a polypeptide sequence set forth in SEQ ID NO:2." The term "a polypeptide sequence of SEQ ID NO:2" encompasses polypeptide subsequence of SEQ ID NO:2. Further, the term "comprising" is open language that opens up the claimed variant to include additional amino acids. Therefore, the resulting polypeptide variant encompassed by the

instant claim recitation includes any polypeptide subsequence of SEQ ID NO:2 having any number of additional amino acids added onto the N- and/or C-terminus of the polypeptide. The specification has not adequately disclosed how to make and/or use the genus of polypeptides encompassed by the instant claim recitation for the diagnostic and therapeutic purposes disclosed by the specification. As such, one of ordinary skill in the art would be required to perform undue experimentation to practice the invention commensurate in scope with the claims. The Examiner suggests amending the claim to recite "a polypeptide variant comprising the polypeptide sequence set forth in SEQ ID NO:2" to overcome this part of the rejection.

It remains the Examiner's position that the specification has not adequately disclosed that the claimed polypeptide variants can be used in a pharmaceutical composition or vaccine. The art of Suck et al. (PTO-892; Reference U) teaches that the instantly claimed polypeptide variants of Phl p 1 with an additional cysteine residue at position 236 are "highly comparable, if not equivalent, as judged by sensitive but robust biochemical and immunological analysis" to natural Phl p 1 (In particular, abstract, 3rd to last paragraph on page 1708, whole document). Focke et al. (PTO-892; Reference V) teaches that Phl p 1 cross-reacts with most grass, corn and monocot-derived group I allergens and that allergens contain binding sites for IgE epitopes that cause acute and chronic manifestation of allergy including rhinoconjunctivitis, bronchial asthma, atopic dermatitis and life-threatening anaphylactic shock (In particular, abstract, second and third paragraphs of introduction). Focke et al. also teaches the need for non-anaphylactic peptides of Phl p 1 in order to provide safe immunotherapy options (In particular, whole document). Since the instantly claimed polypeptide variants exhibit equivalent biochemical and immunological

effects to natural Phl p1, which is highly cross reactive and known to cause the symptoms of allergy and life-threatening anaphylactic shock, it is unpredictable whether the claimed polypeptide variants can be used in a pharmaceutical composition or vaccine. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the polypeptide variant in a pharmaceutical composition or vaccine as claimed, absence of working examples providing evidence which is reasonably predictive that the claimed composition is effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition and vaccine with a reasonable expectation of success.

Substantiating evidence may be in the form of animal tests, which constitute recognized screening procedures with clear relevance to efficacy in humans. See Ex parte Krepelka, 231 USPQ 746 (Board of Patent Appeals and Interferences 1986) and cases cited therein. Ex parte Maas, 9 USPQ2d 1746.

7. Claims 6, 12-15 and 17 *are* rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : the polypeptide of SEQ ID NO:2, the polypeptide of SEQ ID NO:2 with a His tag and the LM and HM fold variants of SEQ ID NO:2.

Applicant is not in possession of: a polypeptide variant of major allergen Phl p 1 from timothy grass which comprises an additional Cys residue compared to the wild type Phl p 1 sequence, said polypeptide variant **comprising a polypeptide sequence set forth in SEQ ID NO: 2**, wherein the additional Cys residue has been introduced by exchange of Ala 236 of claim 6; which exists in various fold forms of claim 12; a fold form rPhl p 1-LM of **the polypeptide variant according to claim 6**, which is obtainable by: (a) overexpressing in a host organism, a fusion protein comprising the rPhl p 1 polypeptide variant and a His tag; (b) denaturing inclusion bodies isolated from the host organism using guanidinium chloride; (c) renaturing dissolved protein on a chelate affinity chromatography column; (d) removing the His tag; (e) employing gel filtration; (f) further purifying using chelate affinity chromatography; (g) isolating the target protein from the flow-through; and (h) further employing gel filtration of claim 13; a fold form rPhl p 1-HM of **the polypeptide variant according to claim 6**, which is obtainable by: (a) overexpressing in a host organism, a fusion protein comprising the rPhl p 1 polypeptide variant and a His tag; (b) denaturing inclusion bodies isolated from the host organism using guanidinium chloride; (c) renaturing dissolved protein on a chelate affinity chromatography column; (d) removing the His tag; (e) employing gel filtration; (f) further purifying using chelate affinity chromatography; (g) eluting the target protein with an imidazole gradient; and (h) further employing gel filtration of claim 14; a vaccine which comprises **the polypeptide variant according to claim 6** and an acceptable carrier of claim 15; and a pharmaceutical composition comprising **a polypeptide variant according to claim 6** and a pharmaceutically acceptable carrier of claim 17 for the same reasons as set forth in the Office Action mailed on 07/22/2008.

Applicant's arguments filed on 11/06/2008 have been fully considered, but are not found persuasive.

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It is the Examiner's position that the specification has not adequately described a polypeptide variant "comprising a polypeptide sequence set forth in SEQ ID NO:2." The term "a polypeptide sequence of SEQ ID NO:2" encompasses polypeptide subsequence of SEQ ID NO:2. Further, the term "comprising" is open language that opens up the claimed variant to include additional amino acids. Therefore, the resulting polypeptide variant encompassed by the instant claim recitation includes any polypeptide subsequence of SEQ ID NO:2 having any number of additional amino acids added onto the N- and/or C-terminus of the polypeptide. The specification has not adequately described the correlation between the structure of the genus of polypeptides encompassed by the instant claim recitation for the diagnostic and therapeutic functions in the specification. The Examiner suggests amending the claim to recite "a

polypeptide variant comprising the polypeptide sequence set forth in SEQ ID NO:2" to overcome this rejection.

8. Claim 23 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 11, 2009
Nora M. Rooney

Patent Examiner

Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644